Economic Evaluation of Screening for Hereditary Hemochromatosis

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Public Health Assessment of Genetic Tests for Screening and Prevention

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Economic Evaluation in Healthcare and Public Health

- Quantitative assessment of expected benefits and costs
  - Identify relevant health outcomes
  - Attach probabilities to outcomes
  - Attach values and costs to outcomes
  - Sum up
- Dueling purposes
  - Objective decision-making
  - Advocacy

Framing an Economic Evaluation

- Choose a policy-relevant question
  - Be specific in describing interventions
  - Consider all relevant alternatives
- Identify audience and perspective
  - Health care system
  - Public health & society
- Include all costs relevant to perspective
- Specify assumptions about health outcomes
  - Include probabilities, not just point estimates
- Address time frame and discounting

Economic Evaluation: Cost-Effectiveness Analysis

- Purpose: Determine least expensive way to achieve outcome
- Partial CEA – outcome of cases detected
  - Assumes earlier detection has benefits
  - Excludes treatment costs
  - Excludes averted costs of care
- Full CEA – health outcomes
  - Calculate net monetary costs and health outcomes for each strategy
  - If one strategy costs less and has better outcomes, it "dominates" other strategies and is "cost saving"
  - If one strategy is both more effective and costs more, calculate cost-effectiveness ratio

Calculating Costs

- Use resource costs, not charges
- Intervention costs
  - All costs, not just costs paid by program
  - Cost components
    - Education and counseling prior to screening
    - Diagnosis and genetic counseling
    - Treatment and monitoring
    - Patient time costs (for societal perspective)
- Disease costs
  - Healthcare costs with and without program
- Discount future year costs to present value (3% per year in U.S., 6% in U.K.)

Calculating Health Outcomes

- Deaths averted or life years gained
- Quality-adjusted life years (QALYs)
  - Metric for both morbidity and mortality
  - Multiply time spent in each health state by health state utility (1=health, 0=death)
- Discount future year outcomes to present value (varies by country)
- Cost-effectiveness analyses recommended to use QALYs (cost-utility analysis), but
  - Whose preferences?
  - How to measure preferences?

Interpretation of Cost-Effectiveness Ratios

- Usual approaches
  - Decision rule
    - If CER > $50,000 per QALY (or LY), cost-effective
    - If CER > $100,000 per QALY, not cost-effective
  - League table
    - Compare CER with accepted programs, e.g., mammography
  - Limitations
- Policy makers must decide acceptable value
  - May vary according to type of intervention
  - May differ for deaths and illness
  - Likely to differ among payers

Addressing Uncertainty

- Establish range of plausible values for each model parameter
- Sensitivity and threshold analyses
- Purposes
  - Determine robustness of conclusion
  - Identify influential parameters
  - Help set priorities for data collection

Issues to Consider in Assessing CEAs

- Who are the analysts? Any bias?
- Was relevant policy question addressed?
- Were appropriate alternatives included?
- Was perspective stated? Correctly followed?
- Were important costs excluded?
- Are cost estimates credible?
- Are assumptions of effectiveness conservative? Evidence-based?
- Did sensitivity analysis vary multiple parameters?
- Are conclusions appropriate? Caveats?

Hereditary Hemochromatosis (HH): Challenges for Mass Screening

- Clinical validity
  - Pentrance of genotypes
  - Expression of phenotypes
- Clinical utility
  - Natural history without screening
- Ethical, legal, and social issues
  - Insurance discrimination
  - Use of transfused blood
  - Unnecessary treatment

Cost-Effectiveness Analyses of Hemochromatosis Screening

- Published CEAs (see list)
  - 7 studies published 1994-1997 reviewed by Grosse & Teutsch (2000)
  - 7 more recent studies 1999-2002
  - All conclude screening for HH is cost-effective
  - All 14 prepared by advocates of screening
- Types of screening evaluated
  - Phenotypic screening
    - Adult men
    - Hospital patients
    - Blood donors
    - Employees
  - Genetic (DNA) screening
    - Cascade screening of relatives
    - Blood donors

Common Pitfalls in HH CEAs

- No clear policy question
  - How will screening be offered and to whom?
  - Will people be screened only once?
- Optimistic assumptions favorable to screening
  - Prevalence
  - Penetrance or expression
  - Uptake of screening
  - Compliance with treatment
- Problems with costs
  - Test costs often understated
  - Counseling and other costs excluded
  - Patient costs excluded
- Ignore other conditions identified (e.g. ID anemia)
- Limited sensitivity analyses

Partial CEA of HH Screening in U.S. (Stave et al. 1999)

- **Protocol**
  - Screen employees having blood drawn for other reasons for iron/transferrin
  - Those with elevated TS and elevated ferritin referred for liver biopsy
- **Assumptions**
  - **Epidemiology**
    - Of 1968 employees screened, 16 screened positive
    - Of 16 referred, 3 received liver biopsy, all diagnosed with HH
    - Assumed gain in life years per case diagnosed: 10
  - **Cost**
    - Liver biopsy and examination $1500
    - Maintenance cost: not considered
- **Results**
  - Cost of screening $27,850 (1968 blood tests and 3 liver biopsies)
  - Cost of screening $14.15 per person
  - Life years gained: 15.2 per 1000 persons screened
  - Cost-effectiveness ratio: $928 per life year gained

Full CEA of HFE Screening in Germany (Schoffski et al. 2000)

- Protocol
  - Screen 25-year-old males for C282Y alleles
  - Homozygotes offered phlebotomy Tx
- Assumptions
  - Epidemiology
    - Prevalence 2.5 per 1000
    - Analytic sensitivity 100%
    - Clinical Sensitivity 90%
    - Specificity 100%
    - Penetrance 10%
    - Life-reducing complication 43%
  - Cost
    - DNA test 5 EUR
    - Maintenance cost 50 EUR per year
- Results
  - Cost of screening 7.26 EUR per person screened
  - Net cost of screening 5.62 EUR per person
  - Life years gained: 1.3 per 1000 persons screened
  - Cost-effectiveness ratio: 4,461 EUR per life year gained

Partial CEA of TS Screening in Norway (Asberg et al. 2002)

- Protocol
  - Screen 30-year-old males for elevated non-fasting transferrin saturation
  - Repeat fasting TS, followed by serum ferritin, confirm by HFE test
- Assumptions
  - Epidemiology
    - Prevalence 7 per 1000
    - Sensitivity of screening 89%
    - Sensitivity of genotyping 100%
    - Specificity for first screen 97.8%
    - Probability of liver cirrhosis 15%
  - Cost
    - First screening test $0.32 (reagents only) or $9.73 (charge)
    - DNA test and clinical exam $167.76
    - Maintenance cost: none assumed
- Results
  - Cost of screening $1.91 or $11.32 per person screened
  - Life years gained: 7.3 per 1000 persons screened
  - Cost-effectiveness ratio: $263 or $1559 per life year gained

Conclusions

- Is population screening for HH cost-effective?
  - Plausible but not proven
  - Better outcomes data needed
  - Realistic screening scenarios needed
  - Objective, rigorous CEA needed, once effectiveness data are available
- How to read published CEAs
  - Be skeptical – caveat lector!
  - Apply criteria for good CEAs
  - Epidemiology is often the weak link
  - Demand evidence of effectiveness